Dynamic expression of the Robo ligand Slit2 in bone marrow cell populations.

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Public Summary:
This article describes research that is aimed at understanding how proteins in the bone marrow environment influences the success of bone marrow transplantation therapies.

Scientific Abstract:
The bone marrow (BM) niche is essential for lifelong hematopoietic stem cell (HSC) maintenance, proliferation and differentiation. Several BM cell types, including osteoblast lineage cells (OBC), mesenchymal stem cells (MSC) and endothelial cells (EC) have been implicated in supporting HSC location and function, but the relative importance of these cell types and their secreted ligands remain controversial. We recently found that the cell surface receptors Robo4 and CXCR4 cooperate to localize HSC to BM niches. We hypothesized that Slit2, a putative ligand for Robo4, cooperates with the CXCR4 ligand SDF1 to direct HSC to specific BM niche sites. Here, we have isolated OBC, MSC and EC by flow cytometry and determined their frequency within the bone marrow and the relative mRNA levels of Slit2, SDF1 and Robo4. We found that expression of Slit2 and SDF1 were dynamically regulated in MSC and OBC-like populations following radiation, while Robo4 expression was restricted to EC. Radiation also significantly affected the cellularity and frequency of both the non-adherent and adherent cells within the BM stroma. These data support a physiological role for Slit2 in regulating the dynamic function of Robo-expressing cells within BM niches at steady state and following radiation.